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Electrographic Exercise Stress Testing and Coronary Arteriography

Correlation Among 114 Men With Chest Pain

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The electrocardiographic response to exercise stress testing (EST) was compared with coronary arteriographic findings in 114 men referred for evaluation of chest pain. The men were divided into two groups: group A (69 men) in whom the coronary arteriograms showed at least one major vessel with greater than 70 percent reduction in cross sectional area, and group B (45 men) in whom there was no evidence of coronary arterial narrowing. In both groups A and B the description of chest pain was judged to be at least consistent with the diagnosis of angina pectoris if not always representing classical angina pectoris. Only men with a positive finding to EST and those with a negative EST response after achieving at least 90 percent of predicted maximum heart rate were included in the calculations. Our results were strikingly similar to those obtained from an extensive review of the literature and showed the following: sensitivity, 80.4 percent; specificity, 88.6 percent; predictive value of a positive test result, 91.1 percent; predictive value of a negative test result, 75.6 percent, and efficiency of the test 83.7 percent.

The maximal EST is a useful predictor of coronary artery disease when a male population is evaluated for chest pain. When a population is selected on some basis other than chest pain (such as elevated lipids or age), EST is a much less useful predictor of coronary artery disease.

CONTROVERSY CONTINUES regarding the clinical usefulness of electrocardiographic exercise stress testing (EST), and its value as a worthwhile tool for the diagnosis of coronary artery disease (CAD) has been seriously questioned. Recent articles in the literature have reported specific groups of patients in whom EST was found to be a poor predictor of CAD. These groups of patients include those with type II hyperlipoproteinemia,[1] asymptomatic men[2] and symptomatic women.[3]

In an effort to gain a better understanding of the clinical usefulness of EST as a predictor of CAD we reviewed our experience in 114 male patients with chest pain in whom treadmill EST and subsequent selective coronary arteriography were done. We found that in men without hypertension complaining of chest pain who were

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ABBREVIATIONS USED IN TEXT
CAD = coronary artery disease
ECG = electrocardiogram
EST = exercise stress testing
PMHR = predicted maximum heart rate

maximally exercised, the postexercise electrocardiographic response was a useful predictor of arteriographically demonstrable CAD.

Patients and Methods

Patients referred for evaluation of chest pain in whom EST and subsequent coronary arteriography were carried out were considered for inclusion in this study. Patients who were hypertensive, had valvular or myocardial disease, had had a previous myocardial infarction, had major resting electrocardiographic abnormalities or were receiving medications known to influence electrocardiographic repolarization were excluded.

Selective coronary arteriography was done using either the Sones or Judkins technique. The arteriograms were exposed on 35 mm film in multiple projections using a Philips 6″ Cesium Iodide Image Intensified System (Philips Medical Systems, Inc., Shelton, CT). The coronary arteriograms were evaluated by two independent observers without knowledge of the EST findings. CAD was judged as present if one or more major coronary vessels had an estimated luminal reduction in cross sectional area of at least 70 percent. Patients classified as normal had *no* suggestion of luminal narrowing in any vessel. Patients with CAD, but not 70 percent luminal narrowing in at least one major vessel, were excluded from the study.

In all, 114 men (mean age 44.6 years; range 23 to 65 years) were entered into the study on the basis of the above criteria, and were divided into two groups on the basis of the results of coronary arteriography. Group A comprised patients in whom coronary arteriograms showed at least one major vessel with greater than 70 percent reduction in cross sectional area. Group B comprised patients in whom there was no evidence of coronary arterial narrowing. In both groups A and B the description of chest pain was judged to be at least consistent with the diagnosis of angina pectoris, though not necessarily always representing classical angina pectoris, and served as the indication for coronary arteriography.

Exercise Stress Testing

Exercise testing was done with patients in the fasting state on a treadmill using the Bruce protocol.*[4] Our goal was to exercise each patient to the point of exhaustion. However, EST was discontinued if the patient complained of significant and limiting chest pain, shortness of breath, lightheadedness or dizziness, or if striking ST segment depression was noted. Standard 12-lead electrocardiograms (ECG) were done before, at 1-minute intervals during, and after the EST. The ECG's were recorded immediately and at 2-minute intervals after exercise for a total of at least eight minutes or until ST segment depression had returned to the resting state. The preexercise and postexercise ECG's were recorded in the supine

*EST according to the method of Bruce employs the principle of uninterrupted multistage treadmill exercise. Each stage lasts three minutes. There is a progressive increase in speed and grade as one moves through the stages.

TABLE 1.—*Exercise Test Results in 69 Men With CAD (Group A) Compared With 45 Men Without CAD (Group B)*

	Number		Mean Age (years)		Chest pain during EST		Max HR Percent PMHR		Time on Treadmill (minutes)	
	A	B	A	B	A	B	A	B	A	B
Positive EST	41 (59%)	4 (9%)	48	39	88%	50%	137 (74%)	186 (99%)	5	10
Negative EST and 90% PMHR	10 (14%)	31 (69%)	42	40	30%	29%	176 (94%)	181 (93%)	10	10
Negative EST but less than 90% PMHR	12 (17%)	8 (18%)	50	38	92%	75%	138 (74%)	155 (82%)	6	10
Borderline EST and 90% PMHR	3 (4%)	2 (4%)	42	44	33%	100%	179 (95%)	175 (93%)	9	8
Borderline EST but less than 90% PMHR	3 (4%)	NONE	52		67%		128 (70%)		4	

CAD = Coronary artery disease
EST = Exercise stress testing
HR = Heart rate
PMHR = Predicted maximum heart rate

TABLE 2.—*Definitions of Statistical Terms*[12]

TP = True positive TN = True negative
FP = False positive FN = False negative

$$\text{Sensitivity} = \frac{TP}{TP+FN}$$

$$\text{Specificity} = \frac{TN}{TN+FP}$$

$$\text{Predictive value of positive test results} = \frac{TP}{TP+FP}$$

$$\text{Predictive value of negative test result} = \frac{TN}{TN+FN}$$

$$\text{Efficiency of test} = \frac{TP+TN}{TP+FP+TN+FN}$$

Incidence—Number of occurrences of a particular kind in any given period of a given population (for example, the incidence of poliomyelitis in Transylvania during 1967 was 4 cases per 100,000 population).

Prevalence—Number of continuing events, regardless of the time of their incidence, occurring simultaneously in any given population (for example, the prevalence of diabetes mellitus in Transylvania on December 1, 1967, was 6.1 percent).

position. Blood pressure was carefully monitored by manual sphygmomanometry throughout the test period.

Exercise Testing Results

The postexercise electrocardiogram was judged as abnormal if there was horizontal or downsloping ST segment depression of 1 mm or more which persisted for at least 0.08 seconds beyond the J point.[5-10] ST segment depressions of 0.5 and 0.75 mm were judged as borderline. ST segment changes of less than 0.5 mm were judged as normal. When a patient had resting ST segment depression, the postexercise ST segment depression was compared with that found in the resting state. In such cases there was only minor resting ST segment depression. Patients without positive EST results were further subdivided depending upon whether or not they achieved 90 percent of predicted maximum heart rate (PMHR) for age and sex. Two observers independently evaluated the EST results. Minor differences in interpretation were resolved by arbitration between these two observers.

Results

In 51 men with significant CAD (group A) there was either an unequivocally positive EST or negative EST after achieving 90 percent of PMHR (Table 1). Therefore, 18 men fell into a nondiagnostic category either because they failed to achieve 90 percent of PMHR or the postexercise ECG showed equivocal changes. The 41 men in whom there was a true positive EST and the 10 men in whom there was a false negative EST defined a sensitivity of 80.4 percent for this population (Tables 2 and 3).

Among the men in whom there were normal selective coronary arteriograms (group B), in four there was a positive EST finding and in 31 a negative EST finding while achieving 90 percent of PMHR (Table 1). In ten men EST results were nondiagnostic either because the patients failed to achieve 90 percent of PMHR or because the postexercise ECG showed equivocal changes. The four men with a false positive EST finding and the 31 men with a true negative EST finding defined a specificity of 88.6 percent for this population (Tables 2 and 3).

Discussion

The controversy surrounding the clinical usefulness of EST is due, in part, to a confusion of concepts and a lack of precise definitions (Table 2). Most commonly, EST is used as a noninvasive indicator of the presence or absence of CAD in patients complaining of chest pain suggestive of

TABLE 3.—*Review of Reports in the Literature Comparing Patients With Coronary Artery Disease Who Underwent Maximal EST With Patients Without Coronary Artery Disease**

	Martin[5] *A*	*Linhart*[6] *B*	*McHenry*[7] *C*	*Kelemen*[8] *D*	*Piessens*[9] *E*	*Ascoop*[10] *F*	*TOTAL*	*Vieweg et al*
True positive	39	57	70	26	20	26	238	41
False positive	4	4	4	1	5	3	21	4
True negative	21	42	76	23	22	49	233	31
False negative	10	14	16	22	18	18	98	10
Sensitivity	79.6%	80.3%	81.4%	54.2%	52.6%	59.1%	70.1%	80.4%
Specificity	84.0%	91.3%	95.5%	95.8%	81.5%	94.2%	91.7%	88.6%
Predictive value of + test	90.7%	93.4%	94.6%	96.3%	80.0%	89.7%	91.9%	91.1%
Predictive value of − test	67.7%	75.0%	86.2%	51.1%	55.0%	73.1%	70.4%	75.6%
Efficiency of test	81.1%	84.6%	88.0%	68.1%	65.7%	78.1%	79.8%	83.7%

EST = exercise stress testing

*Criteria similar to the present report were used to select patients from literature.

angina pectoris. However, EST has also been advocated as a screening test for CAD in apparently asymptomatic persons. The physician responsible for interpretation of the results and clinical significance of the postexercise ECG is presented with a vexing problem; that is, what is the relationship between electrocardiographic evidence of ischemia and coronary arterial anatomy. It is known that patients can have angina pectoris and positive findings on EST in the absence of CAD, as seen in valvular aortic stenosis and idiopathic hypertrophic subaortic stenosis. Moreover, many asymptomatic patients exercised several months after a documented myocardial infarction will have a negative EST. Therefore, EST results would seem to be a better index of myocardial ischemia rather than diseased coronary arterial anatomy, and evaluation of results of EST must be judged in this context. Since CAD is the most prevalent cause of myocardial ischemia in this country, it is to be expected that there is a secondary relationship between an abnormal postexercise ECG and CAD via the common pathway of myocardial ischemia.

The vast majority of our 69 men with CAD (group A) had two and three vessel disease and such cases were evenly distributed among those with positive, negative and equivocal EST findings. Not unexpectedly, the more extensive the CAD the easier it was to provoke positive EST findings. The mean heart rate achieved just before terminating the EST was 152 among those men with one vessel disease and a positive EST. For men with positive EST findings and two vessel or three vessel disease, the comparable heart rates were 139 and 129, respectively. In contrast, the men with a positive EST and normal coronary arteriograms achieved a mean heart rate of 186 just before terminating the EST (Table 1).

In the patients in group B (Table 1) coronary arteriograms were entirely normal without any luminal narrowing. None of these patients had hypertension, valvular or myocardial disease or were receiving medications known to influence myocardial repolarization. Their chest pain was judged to be at least suggestive of angina pectoris.

It has been repeatedly shown that maximal EST provides a higher yield of positive results than submaximal EST, just as the postexercise ECG per se is more useful in predicting CAD than the resting ECG. Accordingly, patients with a positive EST finding or a negative EST finding after achieving 90 percent of PMHR were included in our calculations (Table 3). Such patients were considered to have been maximally stressed and to have unequivocal postexercise ST segment depression. Using these criteria, the sensitivity (ability to recognize significant CAD when it was present) was 80.4 percent. If *all* negative EST results had been used in the calculations instead of only those of the men who had achieved 90 percent of PMHR, the sensitivity would have *decreased* to 65.1 percent. The specificity (ability to exclude any CAD when it was absent) was 88.6 percent. If all negative EST results had been used in the calculations instead of only those of men who had achieved 90 percent of PMHR, the specificity would have *increased* to 93.0 percent. The slight gain in specificity did not counterbalance the pronounced loss in sensitivity by including all negative EST results.

In group A, 18 of 69 men and in group B, 10 of 45 men had equivocal EST results either because they failed to achieve 90 percent of PMHR or their postexercise ST segment depression ranged between 0.5 and 0.75 mm (Table 1). Since neither a positive nor a negative EST result was found in these patients, one should not attempt to show changes in sensitivity or specificity by including such patients. It would be possible to define a "utility index" and include only those patients with a positive EST finding and CAD and those with a negative EST result after achieving 90 percent of PMHR and no CAD. If such an index were used it would be 59 percent in group A and 69 percent in group B.

The literature was reviewed in order to find patients who clinically resembled our own and who had undergone maximal EST and coronary arteriography in order to document the presence or absence of CAD (Table 3).[5-10] The findings in groups A and B were quite similar to those reported. The most striking finding was the paucity of false positive EST findings which provided a high degree of specificity (91.7 percent from the literature versus 88.6 percent for our group) and a high predictive value of a positive test (91.9 percent from the literature versus 91.1 percent for our group) (Table 3). Simply stated, this means that a positive EST result is more indicative of disease than a negative EST result is for the absence of disease in men complaining of chest pain.

It must be remembered that the population under discussion up to this point is a selected population because all were complaining of chest

TABLE 4.—*Accuracy of Exercise Stress Testing as a Function of Prevalence of Coronary Artery Disease*

	*A**	*B†*
True positive	950	95
False positive	450	495
True negative	8,550	9,405
False negative	50	5
Sensitivity	95.0%	95.0%
Specificity	95.0%	95.0%
Predictive value of positive EST	67.9%	16.1%
Predictive value of negative EST	99.4%	99.9%
Efficiency of EST	95.0%	95.0%

EST = exercise stress testing

*A. Assume there is a population of 10,000 with a 10 percent prevalence of coronary artery disease in which the sensitivity and specificity of exercise stress testing are 95 percent.

†B. Assume there is a population of 10,000 with a 1 percent prevalence of coronary artery disease in which the sensitivity and specificity of EST are 95 percent.

pain. Not all patients described classical angina pectoris; however, patients complaining of chest pain provide a population in which one is more likely to find CAD than in a population free of chest pain. Indeed, when a patient complains of chest pain typical of angina pectoris, the correlation with arteriographic CAD approaches 90 percent.[11] As one moves from a population with a high prevalence of CAD to a population with a low prevalence of CAD, the usefulness of EST will change considerably. As noted in Table 4, a change in prevalence of CAD from 10 percent to 1 percent decreases the predictive value of a positive test from 67.9 to 16.1 percent although the sensitivity and specificity of the test in this example are 95 percent. This statistical fact raises serious problems for EST as a screening procedure in asymptomatic persons, particularly in a population with a low prevalence of CAD.

Two recent articles have been widely quoted as depreciating the usefulness of EST in predicting CAD.[1,2] Both articles employed a risk factor other than chest pain to define their populations. In the paper by Borer and co-workers,[1] type II hyperlipoproteinemia was the common denominator and in the paper by Froelicher and associates,[2] asymptomatic patients with resting electrocardiographic repolarization abnormalities were selected for study. Since EST reflects ischemia, and since both of these populations were selected by a factor that correlates less with ischemia than does chest pain, it is not surprising that the results of these two studies differ from our own. The reader must be wary of attempts to predict anatomy rather than ischemia with EST.

We conclude that in an American male population referred for evaluation of chest pain and free from hypertension, valvular or myocardial disease and not receiving medications known to influence electrocardiographic repolarization, EST to an end point of 1 mm ST segment depression or 90 percent of PMHR is a highly useful predictor of associated CAD. That is, chest pain due to myocardial ischemia (angina pectoris) can be distinguished from noncardiac chest pain using maximal EST. It must be recognized that a significant number of patients will fall into a nondiagnostic category either because symptoms develop that preclude their reaching 90 percent of PMHR or because the postexercise-electrocardiographic changes fall into a borderline category between 0.5 and 0.75 mm ST segment depression. It must also be recognized that when a male population is selected on some basis other than for evaluation of chest pain, the maximal EST is much less useful as a predictor of associated CAD.

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